Severe acute dystonia induced by ondansetron in a paediatric patient: a case report

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Abstract

Ondansetron, a 5-HT3 serotonin receptor antagonist, is widely used to manage nausea and vomiting, particularly in postoperative recovery, chemotherapy, and paediatric gastroenteritis. Although it is well-tolerated, recent reports have raised concerns regarding dystonic reactions associated with its use, particularly in children. A 9-year-old boy (24 kg) developed acute dystonia after receiving a 2mg intravenous dose of ondansetron followed by a 4mg oral dose for symptomatic relief of acute gastroenteritis. Several hours post-administration, he exhibited abnormal muscle movement. Clinical examination showed dystonia and a positive Babinski's sign. The patient was diagnosed with ondansetron-induced acute dystonia and was successfully treated with oral trihexyphenidyl and clonazepam. Emerging evidence indicates that ondansetron may disrupt dopaminergic-cholinergic balance in the basal ganglia, potentially triggering dystonic reactions. The Naranjo scale classified this reaction as "probable", further supporting ondansetron as the causative agent. Although rare, dystonic reactions can occur with ondansetron, especially in paediatric populations. Clinicians should remain vigilant when prescribing ondansetron, especially in children.

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Introduction

Ondansetron is a selective 5-HT3 serotonin receptor antagonist, and is widely used for its antiemetic properties in clinical settings. It is primarily prescribed for the management of nausea and vomiting associated with Postoperative Nausea and Vomiting (PONV) and chemotherapy, as approved by FDA.[1] Ondansetron exerts its therapeutic effect by blocking the 5-HT3 receptors, leveraging its structural similarity to serotonin, to provide effective symptom relief. Its application has expanded to include poediatric patients, especially in the treatment of acute gastroenteritis. Ondansetron has few adverse effects and is generally well tolerated.[2]

Generally well-tolerated, ondansetron is associated with minimal side effects.[2] Compared to dopamine antagonist antiemetics, it has a lower risk of extrapyramidal side effects due to its weak affinity for dopamine receptors. This reduces the likelihood of disrupting the dopaminergic-cholinergic balance that regulates posture and involuntary motor functions via acetylcholine, dopamine, and Gamma-Aminobutyric Acid (GABA) within the extrapyramidal tracts. Consequently, symptoms such as rigidity, tremors, and bradykinesia—commonly seen with potent dopamine antagonists—are less frequent. However, caution remains necessary, particularly for patients with pre-existing neurological conditions.[3,4] Recent research has focused on dystonic reactions associated with ondansetron use, especially as it remains the first-line antiemetic for acute gastroenteritis in paediatric patients. Reported adverse effects range from isolated upper extremity chorea to severe whole-body jerking movements.[5]

Case Report

A 9-year-old boy weighing 24 kg presented to the emergency department with the onset of dystonia. He had a prior diagnosis of acute gastroenteritis and had initially reported two episodes of non-bilious, non-projectile vomiting, giddiness and abdominal pain localized to the umbilical region starting the day before admission. He was taken to a local health centre where he received the following medications: Inj. Ondansetron 2 mg (0.08 mg/kg),

Inj. pantoprazole 40 mg, tablet dicyclomine 20 mg and acetaminophen 500 mg and Intravenous Fluid (IVF) 0.9% Dextrose Normal Saline (DNS). Within a few hours, the patient experienced abnormal body movements, prompting his referral to our institution. The patient had no past history of adverse reactions and was not taking any herbal or indigenous drugs. He developed deviation of the mouth towards the left side, rigidity of lower limbs, abnormal neck posture, and brisk reflexes. These symptoms were episodic. Initially, he was alert, conscious, and oriented to time, place, and person. Upon evaluation, his temperature, blood pressure, blood glucose, respiration, and pulse rate were within normal ranges, with no indications of dehydration. There were no focal neurological deficits as per the CT scan performed. However, Babinski's sign was positive (Figure 1) and hypertonia was observed.

Serum electrolytes, urine routine analysis, renal function test, complete blood count, and liver function tests were all within normal limits. At one week of follow-up, the patient remained healthy with no recurrence of dystonic episodes. Based on the Naranjo scale, ondansetron was classified as the probable cause of the acute dystonia. On admission, the patient received an immediate dose of oral trihexyphenidyl 5 mg, oral clonazepam 0.25mg, which alleviated the lower limb stiffness and mouth deviation (Figure 2). The patient was closely monitored for symptoms and potential drug-related adverse effects were assessed. Medication adjustments or additional therapies were considered based on the patient's clinical response. The patient demonstrated significant symptomatic improvement following 72 hours of treatment, therefore all the medications were withdrawn and oral trihexyphenidyl was gradually tapered.The patient has been discharged after exhibiting notable progress.A follow-up appointment was scheduled one week later, during which investigations revealed no abnormalities and no recurrence of dystonic episodes.

Discussion

Ondansetron, a selective 5-HT3 receptor antagonist, prevents nausea and vomiting by blocking serotonergic transmission. It acts at the nucleus tractus solitarius and the chemoreceptor trigger zone in the brain, as well as on vagal nerve terminals in the gastrointestinal tract.[6,7]

Clinical studies have demonstrated the efficacy of ondansetron in managing paediatric gastroenteritis. In a study by Cubeddu *et al.*,[8] children treated with ondansetron or metoclopramide experienced significantly fewer emetic episodes compared to those administered a saline placebo ($p < 0.05$). Similarly, Reeves *et al.*[9] reported that children receiving ondansetron with intravenous fluids were more likely to stop vomiting completely than those who received IV fluids and placebo (70% *vs.* 51%; p=0.04). Furthermore,ondansetron has a relatively mild side effect profile compared to dopamine antagonists and anticholinergics.[10] Though initially believed not to cause extrapyramidal side effects, case reports have documented instances of ondansetron-induced dystonic reactions.[11] This may result from ondansetron's interaction with serotonergic pathways that influence dopaminergic transmission in the basal ganglia and limbic system.[12] By blocking 5-HT3 receptors, ondansetron may indirectly alter dopamine and acetylcholine activity, leading to an imbalance that triggers dystonia.[13,14] The first documented case of ondansetron-induced extrapyramidal symptoms was reported by Dobrow *et al.*,[15] and Diaz-Parlet *et al.* described a severe dystonic reaction requiring intensive care support.[16] Management of ondansetron-induced dystonia involves early symptom recognition and pharmacologic intervention. Anticholinergic agents such as trihexyphenidyl, are effective in alleviating dystonic symptoms by restoring the dopamine-acetylcholine balance.[17] Additionally, benzodiazepines like clonazepam, have shown efficacy in reducing muscle rigidity and associated anxiety in extrapyramidal reactions.[18]

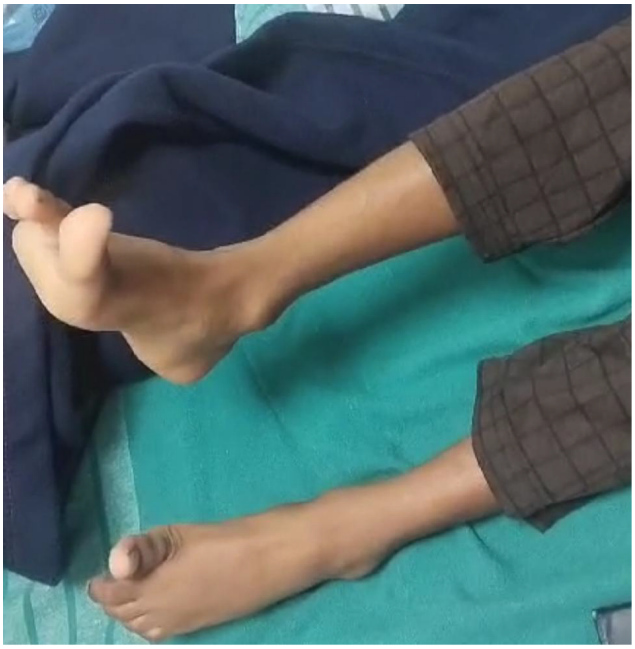

Figure 1. Babinski's sign was positive in this patient after administration with Ondansetron.

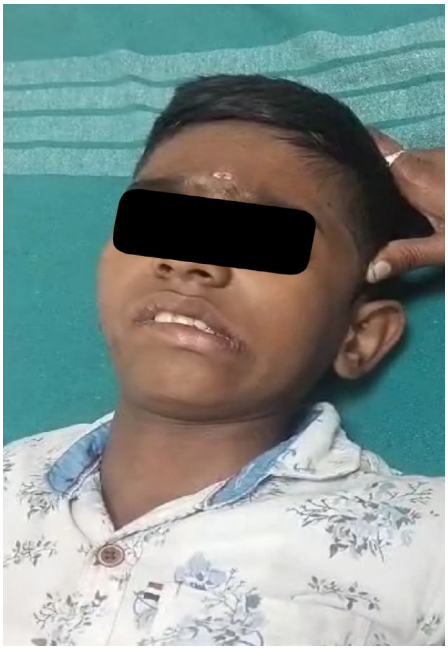

Figure 2. Deviation of mouth was observed in this patient after administration of ondansetron.

Furthermore, the probability that ondansetron caused the dystonic reaction was assessed using Naranjo's Adverse Drug Reaction Probability Scale, a validated instrument for assessing causality by taking into account variables like the patient's response to dechallenge and rechallenge, the known side effect profile of the drug, and the temporal relationship between drug administration and the adverse event. The classification of the reaction as "probable" based on this evaluation supported the theory that ondansetron was the most likely cause of the dystonia.[19] Further investigation is warranted due to the striking similarity between this case and previously reported instances in which ondansetron was associated with dystonic reactions.

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